Aesth. Plast. Surg. 28:45–53, 2004
DOI: 10.1007/s00266-003-3019-9

Aesthetic Plastic Surgery

A Study on Patients Treated with Polyacrylamide Hydrogel Injection for Facial Corrections

Vibeke Breiting, Annet Aasted, Anna Jørgensen, Per Opitz, and Allan Rosetzsky

Denmark and Sweden

Abstract. Polyacrylamide hydrogel (PAAG) has been used as a tissue filler in facial corrective surgery and for breast augmentation in Kiev, Ukraine, for more than 10 years with reportedly very good results. These results, however, have not been published in peer-reviewed journals. A Danish/Swedish group of plastic surgeons with special interest in facial corrective surgery did a retrospective, systematic, pre-planned investigation of 104 patients treated at the center in Kiev. All data were entered into a pre-programmed database for data processing. The mean age of this population was 37.4 years and the mean time since the gel injection was 3.9 years. An average of 5.7 ml of PAAG was injected prior to the investigation. The gel was well tolerated and assessment of the outcome was judged to be very good by 78% and good by 22%, by both physicians and patients. It is concluded that PAAG is well tolerated and seems to be a promising product for facial corrective surgery. Currently, the product (Aquamid®) is being studied in several prospective clinical trials, one of which is completed and in the process of preparation for publication.

Key words: Facial corrective surgery—Polyacrylamide hydrogel (Aquamid®)—Clinical study—Tissue fillers—Lipo- and facial augmentation

Introduction

The use of tissue fillers in facial corrective surgery has become a reality over the last 6 to 8 years. Several techniques have been described for augmenting soft tissues such as fluorinated polymers [1], hydroxyapatite [1], purified autologous collagen [2–6], polymethylmethacrylate microspheres [7], aminocaproic acids [8,9], expanded polytetrafluoroethylene (E-PTFE) [10] and other microparticles as well as autologous fat injections [11–14]. Some of these techniques have been employed with more or less good results because of problems such as migration, reabsorption, scar tissue formation and toxicity.

We have conducted a retrospective study of 104 patients treated with polyacrylamide hydrogel (PAAG) injections for facial correction. The good results we found combined with the convenient mode of administering this product warrants its publication in anticipation of prospective clinical trials, which are being initiated.

Description of Material

Polyacrylamide hydrogel, now marketed as (Aquamid®), is an atoxic, stable, non-resorbable, sterile watery gel for injection into the soft tissues. It consists of approximately 2.5% cross-linked polyacrylamide and non-pyrogenic water. Due to its unique characteristics the gel is highly bio-compatible.

PAAG has been used in plastic and aesthetic surgery in Russia for more than 10 years. Approximately 30,000 patients have been treated with it. Comprehensive data regarding the safety of the gel includes pre-clinical as well as clinical studies.

PAAG is widely used in biomedical research as well as in industry. For decades it has been used in the preparation of soft contact lenses. In biomedical research the product serves as tissue implant material, and it is used in tissue models, body fluid models, detectors of penicillin antibodies, as well as carriers of hormones and drugs in animal studies. In the United States most of the polyacrylamides are used in water and wastewater treatment as a thickening and sus-

Correspondence to Vibeke Breiting, Holte Plastikkirurgiske Klinik, Holte Midtpunkt 20^3 tv., DK-2840 Holte, Denmark

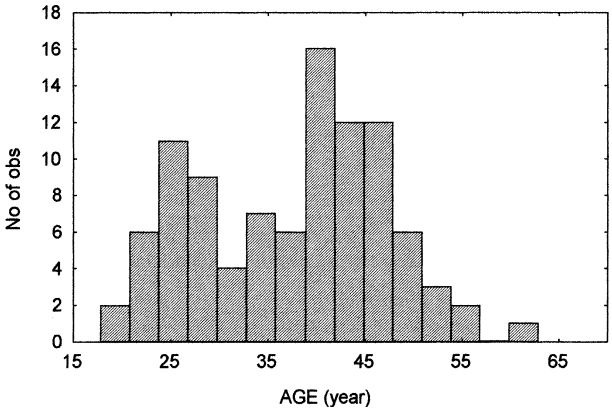

Fig. 1. Patient demographics: frequency distribution of patient age at time of investigation. N = 96, mean ± SD = 37.4 ± 9.7.

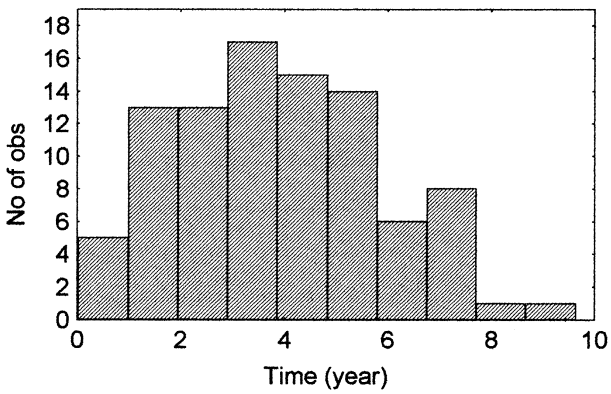

Fig. 2. Demographics: frequency distribution of time (years) from time of last facial correction to date of examination. N = 93, mean time ± SD = 3.9 ± 2.

pending agent. In lesser amounts, polyacrylamide is used in sugar clarification and drug production [14]. Another branch extensively using polyacrylamides is the cosmetic industry [15].

The interest in polyacrylamides originated because of their use in the groundwater clearance. Obviously, chemicals used for the groundwater treatment have to be non-toxic to avoid possible hazards to humans or animals. Comprehensive toxicology studies of polyacrylamides has shown that polyacrylamide is non-toxic to humans as well as animals [16]. Thus, a long-term feeding study (2 years) in dogs and rats with polyacrylamides revealed that there were no specific toxic effects on animals. D. J. King and R. R. Noss from the University of Massachusetts summarize in their review numerous articles reporting toxicology studies with polyacrylamides [17]. They concluded that polyacrylamides are non-toxic when used at a limited range [17].

It is generally believed that the main toxicological concern with polyacrylamide is its acrylamide monomer content [18] which is below 0.0064 μg/ml. Thus, by implantation of PAAG the single dose of

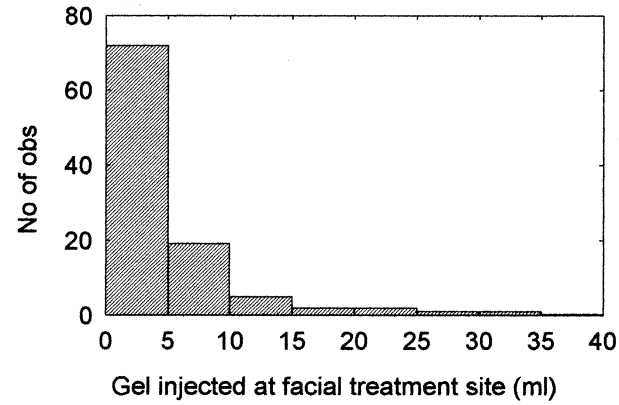

Fig. 3. Demographics: frequency distribution of total ml gel injected for facial correction. N = 93, mean ± SD = 5.7 ± 5.5 ml.

monomer is lower than the exposure to drinking water in 1 or 2 days [19].

The stability as well as toxicity of PAAG has been extensively investigated in Russia (the previous Soviet Union) during the past 10 years and for the Aquamid® formula it has now been confirmed in Denmark in several toxicology studies according to ISO standards (data on file with CONTURA SA). Some investigations were performed also in Norway and USA. The stability of the gel was assessed by various methods, e.g., exposure of the gel to enzymes, bacteria, and oxidizing agents [20,21]. All studies revealed that PAAG is a stable, practically nondegradable product.

In vitro experiments concerning cytotoxicity were performed on cell cultures as well as on human blood cells. No cytotoxic effects were detected after incubation for 24, 48 hours and 10–12 days with PAAG [20,22]. Additionally, no impact on human blood cells was observed after incubation with 5% PAAG for 24 hours [23]. *In vivo* studies were performed on various species including rats, mice, rabbits and dogs. In BALB/c mice, PAAG had no mutagenic effects, as assessed by micronuclei testing [24]. Subchronic toxicology studies in rats revealed no effects on blood and liver biochemistry, and no inflammatory processes were observed [25]. After 6–8 weeks of PAAG injection (s.c.) in rabbits, no physiological or histological changes were observed, and liver and spleen were not affected [26]. No carcinogenic effects have been seen 18 month after implantation of PAAG (i.m.), assayed by immunodetection of organospecific tumor-associated antigens [27].

Histology done on different tissues from various animals as well as from humans after longer time of incubation (6 month - 10 years) have shown that the gel inter-grows with thin inter-layers of connective tissue and elastic fibres [28]. No thick fibrous capsules, dystrophic nor necrotic changes, local allergic reactions, haemodynamic disturbances, carcinogenic effects or calcium salt deposits have been observed

Table 1. emographics: number of corrections at each facial area examined in 96 patients.

	Forehead incl., glabella	Lip augm.	Malar	Naso-labial cleft	Eye-surr.	Nasal area	Other	Total
1st facial cor.	16	48	5	36	0	0	9	114
2nd facial cor.	4	17	4	12	0	0	6	43
3rd facial cor.	2	6	1	6	0	0	2	17
Total areas	22	71	10	54	0	0	17	174

Table 2. Tolerability: frequency of results from examination of skin color, skin thickness and subcutaneous fat at sites of gel injection.

	Diagnosis	Count	%
Skin color	Pale	0	0
	Cyanotic	0	0
	Normal	95	99
	Missing	1	1
	Totals	96	100
Skin thickness	Thin	2	2
	Medium	89	93
	Thick	3	3
	Missing	2	2
	Totals	96	100
Subcutaneous fat	Atrophy*	1	1
	Normal	94	98
	Excessive	0	0
	Missing	1	1
	Totals	96	100

*Congenital hemifacial atrophy.

[28], and gel has not been demonstrated in lymphatic nodes [29–31].

Method of Administration

The gel is injected under local anesthesia, but for correction of wrinkles and folds, local anesthesia is not necessarily required. For lip augmentation, anesthesia through a nerve block is recommended. The procedure must be conducted under sterile conditions. The gel is delivered in pre-filled sterile syringes of 1 ml with Luer lock and should be injected subcutaneously with a thin-gauge needle, e.g., 27 G. The necessary amount of gel is injected subcutaneously in a retrograde manner by injecting the gel while withdrawing the needle. After the injection a light manipulation helps to obtain an even distribution of the gel. The injected gel will form a stable, soft part in the connective tissue. Secondary injections can be given and gel can be aspirated within a year if deemed excessive.

Clinical Experience

Since the 80s a hydrogel consisting of 5% polyacrylamide and 95% water has been used in aesthetic/plastic surgery. Most of the patients treated with PAAG have undergone breast augmentation and/or facial corrections. In 1996 a retrospective clinical study was performed by a group of Danish investigators on 175 patients who were randomly selected from a list of 390 patients who had undergone mammoplasty before 1/7/94 at the clinic in Kiev [32]. The tolerability of the injections, assessed by side effects and the results of laboratory tests, showed that the injection sessions were well tolerated and only a few side effects (2%) were observed. These occurred mostly due to incorrect technique of injection which could be altered, or they were judged not to be related to the gel injection. The overall cosmetic results assessed by surgeons and patients themselves were very good [32].

Material and Methods

The investigation was carried out according to a protocol adapted to Good Clinical Practice (GCP) requirements. The investigational site in Kiev identified from their hospital records all the patients who had had injections of PAAG in the face and invited them by letter to participate. Patients were invited to call the center and arrange for an appointment during weeks 39 and 40, 2000. The clinical investigation was conducted by one or more of four independent specialist surgeons in the presence of an interpreter, and all findings were noted in a pre-printed case report form (CRF). The patients filled in a questionnaire to assess their evaluation of both the cosmetic result and safety of the procedure. Both CRF and patient questionnaire assessed the health status of the patient regarding local (facial) as well as systemic effects/events. Normal aesthetic criteria were used by both surgeons and patients. None of the patients had been examined systematically prior to the injection(s), and no pre-injection photos existed. The photos attached to this study originate from Danish and Swedish patients having received facial injections of PAAG, produced in Denmark under the trade name (Aquamid®) (Figs. 4–8). For all patients the volume of polyacrylamide hydrogel previously injected was recorded. If more than one injection had been administered, the volume of each injection was recorded separately in the CRF. If the patient had had injection of polyacrylamide for breast augmentation, this was recorded as well along with the date and volume

Table 3. Tolerability: frequency of symptoms as judged by examination of the treatment site after facial correction.

	No		Yes		NA		Total	
	Count	%	Count	%	Count	%	Count	%
Depigmentation	95	99	0	0	1	1	96	100
Hyperaemia	92	96	1	1	3	3	96	100
Hyperpigmentation	93	97	2	2	1	1	96	100
Hypertricosis	94	98	0	0	2	2	96	100
Other*	65	68	30	31	1	1	96	100
Peau d'orange	94	98	0	0	2	2	96	100
Polish like skin	93	97	1	1	2	2	96	100
Rash	94	98	0	0	2	2	96	100
Scars	93	97	1	1	2	2	96	100
Scratch marks	94	98	0	0	2	2	96	100
Sebaceous glands hyperplas.	93	97	1	1	2	2	96	100
Teleangiectasia	94	98	1	1	1	1	96	100
Wrinkles	95	99	0	1	1	1	96	100

Note that no symptom contains information from all patients. NA refers to number of patients from whom relevant information to this table was not available.
*Other refers to women in whom the gel was palpable as small firm pearls, mainly in the lips. These pearls were not related to time since injection nor number of injections. They were asymptomatic to the patients and could not be seen on naked eye inspection.

Table 4. Tolerability: frequency of symptoms when palpating the skin area.

Skin sensitivity at injection site	Count	%
Hypersensitivity	4	3
Low sensitivity	1	1
Normal	87	96
NA	4	4
Total	96	100

NA = number of patients from whom relevant information is not available.

injected in order to evaluate the total patient exposure to the product.

The cosmetic result was judged by both the investigator(s) and the patient and rated on an interval scale with four options ranging from very good to very unsuccessful. The safety assessment included the following signs and symptoms, which could possibly be related to the injections: skin color, skin thickness, development of subcutaneous fat, teleangiectasia, depigmentation, wrinkles, hyperpigmentation, peau d'orange, scratch marks, hyperemia, rash, polish-like skin, scars, hypertricosis and sebaceous glands hyperplasia. All of these signs and symptoms were recorded as present or absent. In addition, the skin sensitivity at the injection site was assessed.

The investigators filled in the case report from which included all fields. No patient identifiable data were recorded, just name, date of birth, CRF number, date of investigation and investigators signature which were kept in a log at the study site. After completion of all CRFs, the complete sets were reviewed by a monitor from a Contract Research Organization (CRO) for completeness and legibility and all corrections were entered by the investigators prior to double data entry into the database.

Results

Demographics

The data contained information on 104 patients, however, many records contained no information on one or several of the pre-planned variables. Seven patients did not wish to give day of birth, but their birth year and most other variables were known. These patients, who are not included in the comparative analyses, will be described separately under each heading. One woman failed to report on breast augmentation. As this variable may potentially influence the analyses of tolerability to PAAG, it was decided to exclude her from further analyses.

A total of 96 patients were left to be included in the overall analyses. Their age distribution is illustrated in the frequency histogram presented in Figure 1.

The majority of women belonged to younger age groups. Only a minority (6) were 50 years or older. The 7 women with unknown birth date showed an age span of 30–61 years, with a mean age of 39 years.

Examination of the patients took place from a few months to 9 years after their facial correction, with the majority examined 2–6 years after PAAG injection. The distribution of time since facial correction can be seen in Figure 2.

A majority of women had a follow-up time ranging from 1 1/2 to years. The follow-up time of the 7 women with unknown birth date was from 9 months to 9 years, with a mean time of 3 1/2 years.

The patients received from 1 to 3 facial corrections so that the presented material consists of a total of

Table 5. Tolerability: table of other results when palpating the skin.

	No		Yes		NA		Total	
Measurement item	Count	%	Count	%	Count	%	Count	%
Fluctuation	91	95			5	5	96	100
Haematomas	92	96			4	4	96	100
Migration of gel	88	92	3	3	5	5	96	100
Oedema	90	94	2	2	4	4	96	100
Pain at palpation	90	94	1	1	5	5	96	100
Palpable regional lymph nodes	81	84	10	10	5	5	96	100
Scar tissue	91	95			5	5	96	100
Shrinkage	90	94	1	1	5	5	96	100

Table 6. Tolerability: results of the Mann-Whitney test for differences between patients detected positive for 'Reg. Lymph. Nodes' in age, total amount of gel injected at facial corrections and time since last facial correction.

Variable tested	Z	P-level	No: Count	Yes: Count
Age	−0.67	0.501	81	10
Volume gel injected	−0.08	0.939	81	10
Time since last facial corr.	−0.25	0.802	80	10

Table 7. Treatment results: result of investigator's global assessment of the result of facial corrections.

Investigator's assessment	Count	%
Very good	75	78
Good	20	21
Unsuccessful	1	1
Very unsuccessful	0	0
Totals	96	100

Table 8. Treatment results: result of patient's global assessment of facial correction.

Patient's assessment	Count	%
Very good	75	78
Good	21	22
Unsuccessful	0	0
Very unsuccessful	0	0
Totals	96	100

174 interventions in 96 patients. The distribution according to number of corrections in each patient and the facial site is presented in Table 1.

A total of 49 patients (51%) had had breast augmentation as well, most of these belonging to the group with only 1 facial correction. In the group of 7 women with unknown birth date, 2 also had had breast augmentation. They did not present with any symptoms.

The amount of gel injected for facial correction was recorded and data were available from 93 patients. In Figure 3 it can be seen that the majority received up to 5 ml PAAG. The group of 7 women with unknown birth date did not differ from the main group in number of facial corrections or amount of injected gel.

Table 9. Treatment results: Results when patients were asked "If you were going to need another facial correction would you accept a procedure with injection of PAAG again?"

Patient's assessment	Count	%
No	5	5
Yes	85	89
Perhaps	6	6
Totals	96	100

A special sub-analysis of women with versus women without concurrent breast augmentation with PAAG was performed in order to identify any treatment-related effects of the amount of gel injected, as the volume employed in the breast augmentation procedure is considerably higher than in the facial correction procedure. No correlation was found between women with a large quantity of PAAG injected (simultaneous breast augmentation) and women with only facial gel injections regarding adverse effects or complications (data not shown).

Tolerability

Most variables investigated in the analyses of tolerability showed very small effects due to facial corrections. Though age, previous breast augmentation with PAAG (large amount of gel injected) and amount of gel injected at facial corrections potentially might influence treatment results, this was

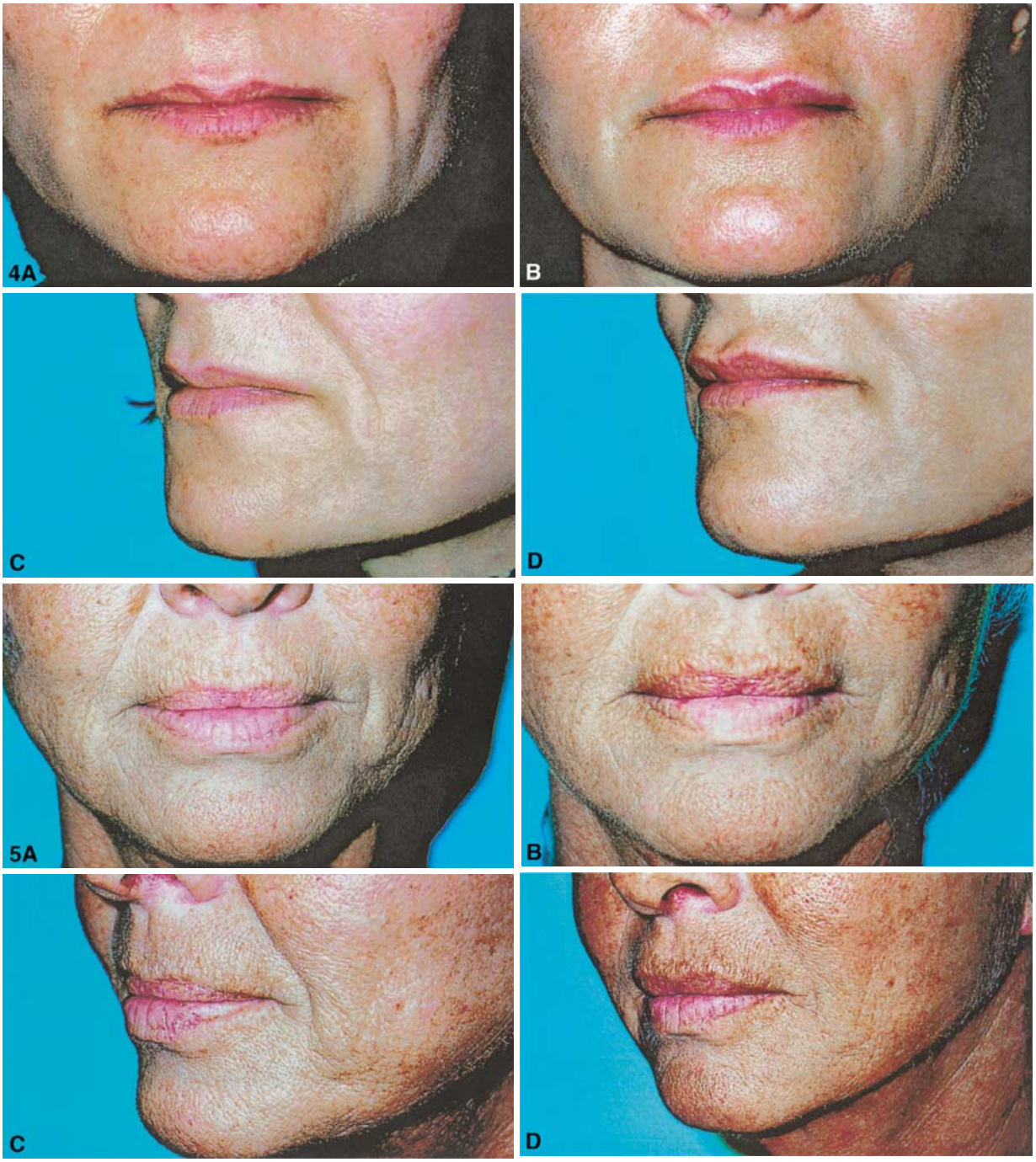

Fig. 4. Upper lip *Citing for figs 4,5,6,7,8?* augmentation with PAAG in a 41-year-old woman. A: front view, before; B: front view, after, C: side view, before; D: side view, after augmentation.
Fig. 5. Upper lip augmentation with PAAG in a 55-year-old woman. A: front view, before; B: front view, after; C: side view, before; D: side view, after augmentation.

generally undetected in the present study. Thus, the very few cases of unwanted treatment effects in most cases render analyses of the above mentioned co-variables meaningless. The findings related to tolerability at physical examination of the injection site in the face are presented in Tables 2, 3, 4 and 5. The Case Record Form required specific examination for 13 other findings. The results are presented in Table 3.

All these examinations demonstrated very good tolerability and low reactivity in the tissues around the sites of injection. No symptoms of the above-mentioned conditions were encountered among the 7 women with unknown birth date.

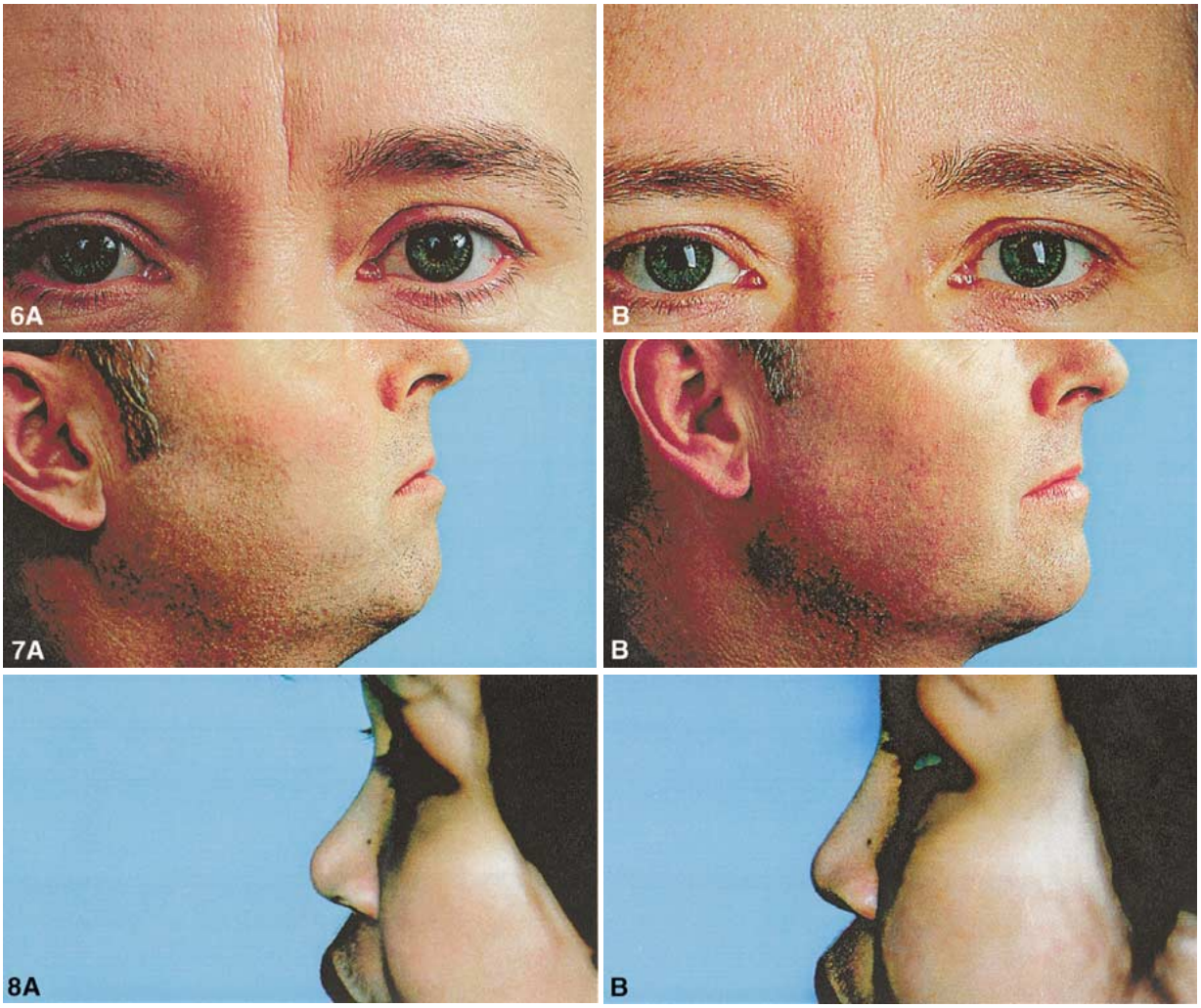

Fig. 6. Glabella augmentation with PAAG in a 42-year old woman. A: front view, before; B: after augmentation.
Fig. 7. Chin augmentation with PAAG in a 50-year-old male; A: side view, before; B: after augmentation.
Fig. 8. Nose-ridge augmentation with PAAG in a 33-year-old oriental woman, side view. A: before; B: after augmentation.

One category (palpatory regional lymph nodes, Table 5) showed a considerable number of Yes answers (approx. 12%). This was, however, not regarded as abnormal, as all of them were small, smooth, rounded and non-adherent. It was also tested if median age, median amount of gel injected at facial correction, and median time (year) since last facial correction would deviate between the 'Yes' and the No' group with respect to this category. The test results appear in Table 6.

The Mann-Whitney test failed to reveal significant *p*-values in all the variables tested. It is therefore concluded that age, total amount of gel injected in facial corrections and time since last facial correction has no effect on the probability of finding palpable regional lymph nodes.

The same test performed with the same variables for probability of having had previous breast augmentation with PAAG did not demonstrate any correlation. In total, apart from the palpable cervical lymph nodes (12%), which we consider to be in accordance with normal incidental findings [33], and the palpatory finding in the lips (small "pearls"), the complication rate was small. Migration of the gel was demonstrated in 3 women, all in connection with the naso-labial fold, but the migration was only a few mm.

Evaluation of Cosmetic Outcome

The evaluation of the cosmetic outcome was done by both the physician and the patient on a fixed scale. The results of the evaluations are presented in Table 7 and those of the patients' evaluations appear in Table 8. The frequencies of responses to the question "If you were going to need another facial correction would you accept a procedure with injection of PAAG again?" are given in Table 9. All 3 types of cosmetic outcome evaluation results from the 7 women were similar to those mentioned in the tables. The cosmetic outcome as

judged by both the patient and the physicians thus seems to be satisfactory and in addition, the result is judged identically by patient and physician.

Conclusions

The present retrospective study with its thorough investigation of a large sample of patients in one center which who had undergone facial correction procedures with injections of polyacrylamide hydrogel has demonstrated that the product injected has been very well tolerated. Despite active search and questioning regarding both local side effects or systemic ones, including any possible intercurrent illness, medical treatment or large volume, we failed to demonstrate any such complications with the injection of polyacrylamide hydrogel.

Regional lymph nodes were palpable in approximately 12% of the women. Palpable cervical lymph nodes is a frequent incidental palpatory finding and in this study there was no association with the 1) age of the patient, 2) time since gel injection or 3) amount of gel injection. The finding was therefore considered unrelated to the facial PAAG injection.

Both the physician and patient rated the outcome of the facial correction procedures to be either very good or good. The examination of the patients took place up to 9 years after the facial correction, thus PAAG also seems to be a durable product for these interventions. The present study has demonstrated that polyacrylamide hydrogel seems to be a well tolerated and effective for facial augmentation. Currently, the product Aquamid® is being studied in several prospective clinical trials, one of which is completed and in the process of preparation for publication.

Acknowledgements. We thank CONTURA SA, Switzerland, for a research grant that made this retrospective study possible and the Contract Research Organisation KLIFO A/S, Denmark for their help with the construction of the Case Record Form and database and the statistical analysis. Mr. Wayne C. Pearson, president of Don Allen photographic studios, New York, is gratefully acknowledged for professional guidance in preparation of the photos.

References

1. Lodde JP: Biomaterial in plastic and maxillofacial surgery. *Ann Chir Plast Esthet* **40:**67, 1995
2. Coleman WP, Lawrence N, Sherman RN, Reed RJ, Pinski KS: Autologous collagen. Lipocytic dermal augmentation. A histopathological study. *J Dermatol Surg Oncol* **19:**1032, 1993
3. Liu B, Xu Z, Lyu R: Experimental and clinical observation on wrinkle correction by medical cosmetic collagen injection. *Chung Kuo I Hsuek Ko Hsueh Yuan Hsueh Pao* **16:**197, 1994
4. Spira M, Liu B, Xu Z, Harrell R, Chahaded H: Human amnion collagen for soft tissue augmentation-biochemical characterizations and animal observation. *J Biomed Mater Res* **28:**91, 1994
5. Xu Z, Liu B, You B, Liu Y, Miao Q: Mechanism of medical collagen for soft tissue augmentation. *Chung Kuo I Hsuek Ko Hsueh Yuan Hsueh Pao* **17:**188, 1995
6. Lemperle G, Hazan-Gauthier N, Lemperle M: PMMA microsperes (Artecoll) for skin and soft tissue augmentation. *Plast Reconstr Surg* **96:**627, 1995
7. Gold MH: The Fibrel mechanism of action study. A preliminary report. *J Dermatol Surg Oncol* **20:**586, 1994
8. Gold MH: Fibrel. *Dermatol Clin* **13:**353, 1995
9. Sherris DA, Larrabee WF: Expanded polytetrafluoroethylene augmentation of the lower face. *Laryngoscope* **106:**658, 1996
10. Davies RE, Guida RA, Cook TA: Autologous free dermal fat graft. Reconstruction of facial contour defects. *Arch Otoralyngol Head Neck Surg* **121:**95, 1995
11. Ersek RA: Transplantation of purified autologous fat: A three-year follow-up is disappointing. *Plast Reconstr Surg* **87:**219, 1991
12. Kononas TC, Bucky LP, Hurley C, May Jr JW: The fate of suctioned and surgically removed fat after reimplantation for soft tissue augmentation: A volumetric and histologic study in the rabbit. *Plast Reconstr Surg* **91:**763, 1993
13. Moscona R, Ullman Y, Har-Shar Y, et al.: Free fat injection for the correction of hemifacial atrophy. *Plast Reconstr Surg* **85:**501, 1989
14. McCollister DD, Hake CL, Sadek SE, Rowe VK: Toxicological investigations of polyacrylamides. *Toxicol Appl Pharmacol* **7:**639, 1965
15. AnonymousFinal report of the safety assessment of polyacrylamide. *J Amer College of Toxicology* **10:**193, 1991
16. Smith EA, Oehme FW: Acrylamide and polyacrylamide: A review of production, use, environmental fate and neurotoxicity. *Rev Environ Health* **9:**215, 1991
17. King DJ, Noss RR: Toxicity of polyacrylamide and acrylamide Monomer. *Rev Environ Health* **8:**3, 1989
18. Silvestro E, Desmarais AM: Toxicity of chemical compounds used for enhanced oil recovery, final report. Contract No. DOE/BC/10014-5. United States Department of Energy. Bartersville, OK, 1980
19. Conway EJ et al: Assessment of the need for, and character of limitations on acrylamide and its compounds. Us Environmental Protection Agency Contract No.68-01-4308. USEPA, Office of toxic substances, Washington DC, 1979
20. Bertheussen K: Report from biological test of Royamid in cell cultures, 1998
21. Rul YV, Kovanskaya VA: Report on medicobiological assessment of hydrogel PAAG "Interfall", 1993
22. Cherednichenko VM: Results of study interaction process between hydrophylic gel (PAA) "interfall" and tissues of organisms of experimental animals while implanting, 1993
23. Kogut G: Investigation concerning hemolytic activity of preparation "Interfall", 1994
24. Galatenko NA: Assessment of cytogenotoxic (mutagenous), cytotoxic and cytostatic activity of the acrylamide and commercial samples of polyacrylamide hydrogel PAAG "Interfall" by means of a micronuclear test, 1995

25. Tsvilikhovsky NI, Melnichuk SD: Study of principal biochemical and cytological indices of blood of rats in two weeks after intraperitoneal injection of polyacrylamide gel, 1994
26. Sosa J, Wayne Smith A, Jackson IT: *The use of Royamid (polyacrylamide) in soft tissue augmentation: An experimental assessment*. (Abstract) The European Association of Plastic Surgery, Amsterdam, 1997
27. Novichenko NL: Determination of a potential carcinogenic activity of polyacrylamide gel by methods of immunodetection of organospecific tumour-associated antigens, 1992
28. Christensen LH, Breiting VB, Aasted A, Jørgensen A, Kebuladze I: Long-term effects of polyacrylamide hydrogel (PAAG, Interfall/Contura SA) in human breast tissue. *Plast Reconstruct Surg* **111:**1883, 2003
29. Galatenko NA: Results of study interaction process between hydrophylic gel (PAAG) ''Interfall'' and tissues of organs of experimental animals while implanting, 1993
30. Galatenko NA: Toxicological estimation of hydrogel PAAG ''Interfall'' as an implant, 1992
31. Grigorieva NN, Ischenko I: Structural-functional characteristics of organs and tissues under injection of polyacrylamide gel ''Interfall'' in clinic and experiment, 1991
32. Ryttig KR, Schiøtz J, Jørgensen A: Clinical study report dated 03.01.1998, 1998
33. Steinkamp HJ, Zwicker C, Langer M, Mathe M, Ehritt C, Neumann FR: Reactive enlargement of cervical lymph nodes and cervical lymph node metastases: Sonography (M/Q quotient) and computed tomography. *Aktuelle Radiol* **2:**188, 1992